SEQUENCE LISTING

<110> VERTEX PHARMACEUTICALS, INC. et al.

<120> CRYSTAL STRUCTURES OF JNK-INHIBITOR COMPLEXES AND BINDING POCKETS THEREOF

<130> VPI/02-01PCT

<140>
<141>

<150> 60/348,002
<151> 2002-01-11

<160> 7

<170> PatentIn Ver. 2.1

<210> 1
<211> 422
<212> PRT
<213> Homo sapiens

<400> 1

```
Met Ser Leu His Phe Leu Tyr Tyr Cys Ser Glu Pro Thr Leu Asp Val
  1               5                  10                  15

Lys Ile Ala Phe Cys Gln Gly Phe Asp Lys Gln Val Asp Val Ser Tyr
             20                  25                  30

Ile Ala Lys His Tyr Asn Met Ser Lys Ser Lys Val Asp Asn Gln Phe
         35                  40                  45

Tyr Ser Val Glu Val Gly Asp Ser Thr Phe Thr Val Leu Lys Arg Tyr
     50                  55                  60

Gln Asn Leu Lys Pro Ile Gly Ser Gly Ala Gln Gly Ile Val Cys Ala
 65                  70                  75                  80

Ala Tyr Asp Ala Val Leu Asp Arg Asn Val Ala Ile Lys Lys Leu Ser
                 85                  90                  95

Arg Pro Phe Gln Asn Gln Thr His Ala Lys Arg Ala Tyr Arg Glu Leu
            100                 105                 110

Val Leu Met Lys Cys Val Asn His Lys Asn Ile Ile Ser Leu Leu Asn
        115                 120                 125

Val Phe Thr Pro Gln Lys Thr Leu Glu Glu Phe Gln Asp Val Tyr Leu
    130                 135                 140

Val Met Glu Leu Met Asp Ala Asn Leu Cys Gln Val Ile Gln Met Glu
145                 150                 155                 160

Leu Asp His Glu Arg Met Ser Tyr Leu Leu Tyr Gln Met Leu Cys Gly
                165                 170                 175
```

```
Ile Lys His Leu His Ser Ala Gly Ile Ile His Arg Asp Leu Lys Pro
            180                 185                 190

Ser Asn Ile Val Val Lys Ser Asp Cys Thr Leu Lys Ile Leu Asp Phe
        195                 200                 205

Gly Leu Ala Arg Thr Ala Gly Thr Ser Phe Met Met Thr Pro Tyr Val
    210                 215                 220

Val Thr Arg Tyr Tyr Arg Ala Pro Glu Val Ile Leu Gly Met Gly Tyr
225                 230                 235                 240

Lys Glu Asn Val Asp Ile Trp Ser Val Gly Cys Ile Met Gly Glu Met
                245                 250                 255

Val Arg His Lys Ile Leu Phe Pro Gly Arg Asp Tyr Ile Asp Gln Trp
            260                 265                 270

Asn Lys Val Ile Glu Gln Leu Gly Thr Pro Cys Pro Glu Phe Met Lys
        275                 280                 285

Lys Leu Gln Pro Thr Val Arg Asn Tyr Val Glu Asn Arg Pro Lys Tyr
    290                 295                 300

Ala Gly Leu Thr Phe Pro Lys Leu Phe Pro Asp Ser Leu Phe Pro Ala
305                 310                 315                 320

Asp Ser Glu His Asn Lys Leu Lys Ala Ser Gln Ala Arg Asp Leu Leu
                325                 330                 335

Ser Lys Met Leu Val Ile Asp Pro Ala Lys Arg Ile Ser Val Asp Asp
            340                 345                 350

Ala Leu Gln His Pro Tyr Ile Asn Val Trp Tyr Asp Pro Ala Glu Val
        355                 360                 365

Glu Ala Pro Pro Pro Gln Ile Tyr Asp Lys Gln Leu Asp Glu Arg Glu
    370                 375                 380

His Thr Ile Glu Glu Trp Lys Glu Leu Ile Tyr Lys Glu Val Met Asn
385                 390                 395                 400

Ser Glu Glu Lys Thr Lys Asn Gly Val Val Lys Gly Gln Pro Ser Pro
                405                 410                 415

Ser Ala Gln Val Gln Gln
            420


<210> 2
<211> 340
<212> PRT
<213> Homo sapiens

<400> 2
Phe Tyr Arg Gln Glu Leu Asn Lys Thr Ile Trp Glu Val Pro Glu Arg
  1               5                  10                  15
```

Tyr Gln Asn Leu Ser Pro Val Gly Ser Gly Ala Tyr Gly Ser Val Cys
20 25 30

Ala Ala Phe Asp Thr Lys Thr Gly Leu Arg Val Ala Val Lys Lys Leu
35 40 45

Ser Arg Pro Phe Gln Ser Ile Ile His Ala Lys Arg Thr Tyr Arg Glu
50 55 60

Leu Arg Leu Leu Lys His Met Lys His Glu Asn Val Ile Gly Leu Leu
65 70 75 80

Asp Val Phe Thr Pro Ala Arg Ser Leu Glu Glu Phe Asn Asp Val Tyr
85 90 95

Leu Val Thr His Leu Met Gly Ala Asp Leu Asn Asn Ile Val Lys Cys
100 105 110

Gln Lys Leu Thr Asp Asp His Val Gln Phe Leu Ile Tyr Gln Ile Leu
115 120 125

Arg Gly Leu Lys Tyr Ile His Ser Ala Asp Ile Ile His Arg Asp Leu
130 135 140

Lys Pro Ser Asn Leu Ala Val Asn Glu Asp Cys Glu Leu Lys Ile Leu
145 150 155 160

Asp Phe Gly Leu Ala Arg His Thr Asp Asp Glu Met Thr Gly Tyr Val
165 170 175

Ala Thr Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Trp Met His
180 185 190

Tyr Asn Gln Thr Val Asp Ile Trp Ser Val Gly Cys Ile Met Ala Glu
195 200 205

Leu Leu Thr Gly Arg Thr Leu Phe Pro Gly Thr Asp His Ile Asp Gln
210 215 220

Leu Lys Leu Ile Leu Arg Leu Val Gly Thr Pro Gly Ala Glu Leu Leu
225 230 235 240

Lys Lys Ile Ser Ser Glu Ser Ala Arg Asn Tyr Ile Gln Ser Leu Thr
245 250 255

Gln Met Pro Lys Met Asn Phe Ala Asn Val Phe Ile Gly Ala Asn Pro
260 265 270

Leu Ala Val Asp Leu Leu Glu Lys Met Leu Val Leu Asp Ser Asp Lys
275 280 285

Arg Ile Thr Ala Ala Gln Ala Leu Ala His Ala Tyr Phe Ala Gln Tyr
290 295 300

His Asp Pro Asp Asp Glu Pro Val Ala Asp Pro Tyr Asp Gln Ser Phe
305 310 315 320

Glu Ser Arg Asp Leu Leu Ile Asp Glu Trp Lys Ser Leu Thr Tyr Asp

325 330 335

Glu Val Ile Ser
340

<210> 3
<211> 342
<212> PRT
<213> Homo sapiens

<400> 3
Ala Gly Pro Glu Met Val Arg Gly Gln Val Phe Asp Val Gly Pro Arg
1 5 10 15

Tyr Thr Asn Leu Ser Tyr Ile Gly Glu Gly Ala Tyr Gly Met Val Cys
20 25 30

Ser Ala Tyr Asp Asn Val Asn Lys Val Arg Val Ala Ile Lys Lys Ile
35 40 45

Ser Pro Phe Glu His Gln Thr Tyr Cys Gln Arg Thr Leu Arg Glu Ile
50 55 60

Lys Ile Leu Leu Arg Phe Arg His Glu Asn Ile Ile Gly Ile Asn Asp
65 70 75 80

Ile Ile Arg Ala Pro Thr Ile Glu Gln Met Lys Asp Val Tyr Ile Val
85 90 95

Gln Asp Leu Met Glu Thr Asp Leu Tyr Lys Leu Leu Lys Thr Gln His
100 105 110

Leu Ser Asn Asp His Ile Cys Tyr Phe Leu Tyr Gln Ile Leu Arg Gly
115 120 125

Leu Lys Tyr Ile His Ser Ala Asn Val Leu His Arg Asp Leu Lys Pro
130 135 140

Ser Asn Leu Leu Leu Asn Thr Thr Cys Asp Leu Lys Ile Cys Asp Phe
145 150 155 160

Gly Leu Ala Arg Val Ala Asp Pro Asp His Asp His Thr Gly Phe Leu
165 170 175

Thr Glu Tyr Val Ala Thr Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu
180 185 190

Asn Ser Lys Gly Tyr Thr Lys Ser Ile Asp Ile Trp Ser Val Gly Cys
195 200 205

Ile Leu Ala Glu Met Leu Ser Asn Arg Pro Ile Phe Pro Gly Lys His
210 215 220

Tyr Leu Asp Gln Leu Lys His Ile Leu Gly Ile Leu Gly Ser Pro Ser
225 230 235 240

Gln Glu Asp Leu Asn Cys Ile Ile Asn Leu Lys Ala Arg Asn Tyr Leu

245 250 255

Leu Ser Leu Pro His Lys Asn Lys Val Pro Trp Asn Arg Leu Phe Pro
260 265 270

Asn Ala Asp Ser Lys Ala Leu Asp Leu Leu Asp Lys Met Leu Thr Phe
275 280 285

Asn Pro His Lys Arg Ile Glu Val Glu Gln Ala Leu Ala His Pro Tyr
290 295 300

Leu Glu Gln Tyr Tyr Asp Pro Ser Asp Glu Pro Ile Ala Glu Ala Pro
305 310 315 320

Phe Lys Phe Asp Met Glu Leu Asp Asp Leu Pro Lys Glu Lys Leu Lys
325 330 335

Glu Leu Ile Phe Glu Glu
340

<210> 4
<211> 256
<212> PRT
<213> Mus musculus

<400> 4
Asp Gln Phe Asp Arg Ile Lys Thr Leu Gly Thr Gly Ser Phe Gly Arg
1 5 10 15

Val Met Leu Val Lys His Lys Glu Ser Gly Asn His Tyr Ala Met Lys
20 25 30

Ile Leu Asp Lys Gln Lys Val Val Lys Leu Lys Gln Ile Glu His Thr
35 40 45

Leu Asn Glu Lys Arg Ile Leu Gln Ala Val Asn Phe Pro Phe Leu Val
50 55 60

Lys Leu Glu Phe Ser Phe Lys Asp Asn Ser Asn Leu Tyr Met Val Met
65 70 75 80

Glu Tyr Val Ala Gly Gly Glu Met Phe Ser His Leu Arg Arg Ile Gly
85 90 95

Arg Phe Ser Glu Pro His Ala Arg Phe Tyr Ala Ala Gln Ile Val Leu
100 105 110

Thr Phe Glu Tyr Leu His Ser Leu Asp Leu Ile Tyr Arg Asp Leu Lys
115 120 125

Pro Glu Asn Leu Leu Ile Asp Gln Gln Gly Tyr Ile Gln Val Thr Asp
130 135 140

Phe Gly Phe Ala Lys Arg Val Lys Gly Arg Thr Trp Thr Leu Cys Gly
145 150 155 160

Thr Pro Glu Tyr Leu Ala Pro Glu Ile Ile Leu Ser Lys Gly Tyr Asn

165 170 175

Lys Ala Val Asp Trp Trp Ala Leu Gly Val Leu Ile Tyr Glu Met Ala
180 185 190

Ala Gly Tyr Pro Pro Phe Phe Ala Asp Gln Pro Ile Gln Ile Tyr Glu
195 200 205

Lys Ile Val Ser Gly Lys Val Arg Phe Pro Ser His Phe Ser Ser Asp
210 215 220

Leu Lys Asp Leu Leu Arg Asn Leu Leu Gln Val Asp Leu Thr Lys Arg
225 230 235 240

Phe Gly Asn Leu Lys Asp Gly Val Asn Asp Ile Lys Asn His Lys Trp
245 250 255

<210> 5
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 5
gctctagagc tccatgggca gcaaaagcaa agttgacaa 39

<210> 6
<211> 37
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 6
tagcggatcc tcattctgaa ttcattactt ccttgta 37

<210> 7
<211> 21
<212> PRT
<213> Homo sapiens

<400> 7
Lys Arg Glu Leu Val Glu Pro Leu Thr Pro Ser Gly Glu Ala Pro Asn
1 5 10 15

Gln Ala Leu Leu Arg
20